CHAPTER 32
HUMAN BIOLOGY

HUMAN RADIATION RESPONSE

Effects of X-rays on Human
- *Result of:* interaction at the atomic level

Molecular Change
- *Caused:* deposition of energy in tissue

At each stage, it is possible to repair radiation damage & recover!

HUMAN RESPONSES TO IONIZING RADIATION

EARLY EFFECTS OF RADIATION ON HUMANS

1. Acute radiation syndrome
    a. Hematologic syndrome
    b. Gastrointestinal syndrome
    c. Central nervous system syndrome
2. Local tissue damage
    a. Skin
    b. Gonads
    c. Extremities
3. Hematologic depression
4. Cytogenetic damage

LATE EFFECTS OF RADIATION ON HUMAN

1. Leukemia
2. Other malignant disease
    a. Bone cancer
    b. Lung cancer
    c. Breast cancer
3. Local tissue damage
    a. Skin
    b. Gonads
    c. Eyes
4. Shortening of lifespan
5. Genetic damage
    a. Cytogenetic damage
    b. Doubling of dose
    c. Genetically significant dose

EFFECTS OF FETAL IRRADIATION

1. Prenatal death
2. Neonatal death
3. Congenital malformation
4. Childhood malignancy
5. Diminished growth & development

Early Effect of Radiation
- Radiation response occurs within minutes or days after radiation exposure

Late Effect of Radiation
- Radiation response that is not observe for 6 months or longer after radiation exposure

Radiobiology
- The study of the effects of ionizing radiation on biologic tissue

COMPOSITION OF THE BODY

Atomic Composition
- It determines the character & degree of the radiation interaction that occurs

ATOMIC COMPOSITION OF THE BODY

- 60.0 % hydrogen
- 25.7 % oxygen
- 10.7 % carbon
- 2.4 % nitrogen
- 0.2 % calcium
- 0.1 % phosphorus
- 0.1 % sulfur
- 0.8 % trace elements

CELL THEORY

Robert Hooke (1665)
- First named the cell as the biologic building block

Anton Van Leeuwenhoek (1673)
- Accurately described a living cell on the basis of his microscopic observations

Schneider & Schwann (1838)
- Showed that cells are the basic functional units in all plants & animals

Watson & Crick (1953)
- Described the molecular structure of deoxyribonucleic acid (DNA) as genetic substance of the cell

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Human Genope Project (2000)
- *Result:* precise mapping of 40,000 human genes

Molecular & Tissue Composition
- It defines the nature of radiation response
- *Macromolecules:* proteins, lipids (fats), carbohydrates (sugars & starches) & nucleic acids
- *Principal Organic Molecules:* proteins, lipids & carbohydrates

MOLECULAR COMPOSITION OF THE BODY
- 80.0 % water
- 15 % protein
- 2 % lipids
- 1 % carbohydrates
- 1 % nucleic acid
- 1 % other

Macromolecules
- Very large molecules that sometimes consist of hundreds of thousands of atoms

Organic Molecule
- Life-supporting & contains carbon

Nucleic Acid
- The rarest molecule in the body
- Concentrated in the nucleus of a cell (DNA)
- The most critical & radiosensitive target molecule

Water
- The simplest & the most abundant molecular constituent in the body
- *Important Role:* delivering energy to the target molecules (contribute to radiation effects)
- *Composition:* two atoms of Hydrogen & 1 atom of Oxygen
- *Functions:*
  - Provide some form & shape
  - Assist in maintaining body temperature
  - Enter into some biochemical reactions

Trace Elements & Inorganic Salts
- Essential for proper metabolism

Homeostasis
- The state of equilibrium among tissue & organs

Catabolism
- Breaking down into smaller units of macromolecules

Anabolism
- The production of large molecules from small

Metabolism
- Catabolism & anabolism

Proteins
- Long chain macromolecules that consist of a linear sequence of amino acids connected by peptide bonds
- *Protein Synthesis:* used 22 amino acids
- *Linear Sequence/Arrangement:*
  - AA—AA—AA—AA
- *General Formula:* $C_nH_nO_nN_nT_n$
- *Functions:*
  - Provide structure & support (muscles)
  - Enzymes, hormones & antibodies

Protein Synthesis
- The metabolic production of proteins

Enzymes
- Molecules that are necessary in small quantities to allow a biochemical reaction to continue, even though they do not directly enter into the reaction

Hormones
- Molecules that exercise regulatory control over some body functions

- They are produced & secreted by endocrine glands
- *Endocrine Glands:* pituitary, adrenal, thyroid, parathyroid, pancreas & gonads

Antibodies
- A primary defense mechanism of the body against infection & disease

Antigen
- Invasive & infectious agent

Lipids
- Organic macromolecules composed solely of carbon, hydrogen, & oxygen
- *General Formula:* $C_nH_nO_n$
- *Structural Configuration:* represented by oleic acid molecules
- *Two Types of Molecules:*
  - Glycerol – 1 molecule
  - Fatty acid – 3 molecules
- *Functions:*
  - Thermal insulator from environment
  - Fuel for the body by providing energy stores

Carbohydrates
- Similar to lipids but their structure is different
- First considered to be watered or hydrated carbons
- It is also called *saccharides*
- *Sugars:* monosaccharides & disaccharides
- *Chief Function:*
  - To provide fuel for cell metabolism
- Function:
  - Provide shape & stability

Glucose
- A simple sugar
- The ultimate molecule that fuels the body
- *Chemical Formula:* $C_6H_{12}O_6$

Sucrose
- Ordinary table sugar
- *Chemical Formula:* $C_{12}H_{22}O_{11}$

Polysaccharides
- Plant *starches* & animal *glycogen*
- *Chemical Formula:* $(C_6H_{10}O_5)_n$

Glycogen
- A human polysaccharide
- It stored in tissues of the body
- It used only when quantities of the simple sugar (glucose) are inadequate

Nucleic Acids
- A very large and extremely complex macromolecules
- *Two Principal Nucleic Acids:* DNA & RNA
- *Function:* growth & development of the cell (*protein synthesis*)

Deoxyribonucleic Acid (DNA)
- The control center for life
- It contains all the hereditary information that represents a cell or whole individual (*germ cell*)
- *Location:* nucleus
- *Function:* it serves as the command or control molecule for cell function
- *Sugar Component:* deoxyribose
- *Base Component*: thymine
- *Configuration:* doble-helix

DNA is the radiation-sensitive target molecule!

Nitrogenous Organic Bases
- Attached to each deoxyribose molecule
- *Purines:* adenine & guanine
- *Pyramidines:* thymine & cytosine
- *Sequence of Base Bonding in DNA:*
  - Adenines bonded to thymines
  - Cytosines bonded to guanines

Only adenine-thymine & cytosine-guanine base bonding is possible in DNA!

Nucleotide
- The base sugar-phosphate combination

Ribonucleic Acid (RNA)
- *Principal Location:* cytoplasm
- *Two Types:* messenger RNA & transfer RNA
- *Sugar Component:* ribose
- *Base Component:* uracil
- *Configuration:* single-helix

THE HUMAN CELL

Two Major Structures
- Nucleus & Cytoplasm

Nucleus
- The center of the cell
- Principal Molecular Components:
  - DNA – the genetic material of the cell
- Other Molecular Components:
  - Some RNA, protein, & water

Nucleolus
- A rounded structure that is attached to the nuclear membrane
- It contained most of the RNA

Nuclear Membrane
- A double-walled structure that at some locations is connected to the endoplasmic reticulum

Cytoplasm
- The bulk of the cell
- It contains great quantities of all molecular components except DNA

Endoplasmic Reticulum
- a channel or series or channels that allows the nucleus to communicate with the cytoplasm

Mitochondria
- The large bean-shaped structures
- The engine of the cell

Ribosomes
- The small, dot-like structures
- The site of protein synthesis
- Essential to normal cellular function
- Scattered throughout the cytoplasm or the endoplasmic reticulum

Lysosomes
- The small, pea-like sacs
- They contains enzymes capable of digesting cellular fragments & sometimes the cell itself
- They help to control intracellular contaminants

1 Mrad (10 kGy_t)
- Required to produce a measurable change in any physical characteristic of the molecule

Single-Cell Organism
- *Lethal Dose:* measured in kilorads

Human Cells
- *Lethal Dose:* < 100 rad (1 Gy_t)

Cell Function
- Absorbs all nutrients through the cell membrane

Protein Synthesis
- A critical cellular function necessary for survival

Codon
- A series of three-base pairs
- It identifies one of the 22 amino acids available for protein synthesis

Cell Proliferation
- The act of a single cell or group of cells to reproduce & multiply in number

Two General Types of Cells in the Human Body
- Genetic/Germ Cells
  - Oogonium (female) & spermatogonium (male)

  - They undergo meiosis
- Somatic Cells
  - All cells in the body except oogonium & spermatogonium
  - They undergo mitosis

Mitosis
- Process of somatic cell division wherein a parent cell divides to form two daughter cells identical to the parent cell
- *Four Subphases:* prophase, metaphase, anaphase & telophase (PMAT)

Two Phases of the Cell Cycle (Geneticist)
- Metaphase (M) & interphase

Interphase
- The portion of the cell between mitotic events
- The period of growth of the cell between divisions

Four Phases of the Cell Cycle (Cell Biologist)
- M, G_1, S & G_2

G_1 Phase
- Pre-DNA synthesis phase
- The gap in cell growth between M & S

S Phase
- The DNA-synthesis phase
- *DNA:* replicated into two identical daughter DNA molecules
- *Chromosome:* replicate form a two-chromatid structure to a four-chromatid structure

G_2 Phase
- The post-DNA synthesis gap of the cell growth

Interphase
- *Chromosome:* not visible

Mitosis
- *Chromosomes:* become visible, divide & migrate to daughter cells
- *DNA:* slowly takes the form of the chromosomes as seen microscopically

Prophase
- The nucleus swells
- *DNA:*
  - Becomes more prominent
  - Begins to take structural form

Metaphase
- *Chromosomes:* appear & lined up along the equator of the nucleus
- Mitosis can be stopped
- Chromosomes can be studied carefully under the microscope

Radiation-induced chromosome damage is analyzed during metaphase!

Anaphase
- *Chromosomes:*
  - Each splits at the centromere
  - New chromosome migrates toward the spindle
- Centromere & chromatids are connected by a fiber to the poles of a nucleus
- *Spindles:* the poles
- *Spindle Fibers:* the fibers
- The number of chromatid per centromere is reduced by half

Telophase
- The final segment of mitosis
- Characterized by the disappearance of structural chromosomes into a mass of DNA
- The closing off of the nuclear membrane like a dumbbell into two nuclei
- Cytoplasm is divided into two equal parts

Meiosis
- The process whereby genetic cells undergo reduction division

- *Second Division:* not accompanied by S phase
    - *Result:* no replication

Crossover

- Process that occurs during meiosis wherein chromatids exchange chromosomal material

TISSUE AND ORGANS

Tissue

- Collection of cells of similar structure & function

TISSUE COMPOSITION OF THE BODY

TISSUE	ABUNDANCE
Muscle	43%
Fat	14 %
Organs	12 %
Skeleton	10 %
Blood	8 %
Subcutaneous tissue	6 %
Bone marrow	4 %
Skin	3 %

Organs

- Collection of tissues of similar structure & function

Organ System

- Combination of tissues & organs that forms an overall integrated organization
- *Principal Organ Systems:*
    - Nervous, Reproductive, Digestive, Respiratory & Endocrine

Immature Cells

- Undifferentiated cells, precursor cells or stem cells

Stem cells are more sensitive to radiation than mature cells!

Types of Tissues

- Epithelium, Connective & Supporting, Muscle & Nervous

RESPONSE TO RADIATION IS RELATED TO CELL TYPE

Radiosensitivity	Cell Type
High	Lymphocytes
	Spermatogonia
	Erythroblasts
	Intestinal crypt cells
Intermediate	Endothelial cells
	Osteoblasts
	Spermatids
	Fibroblasts
Low	Muscle cells
	Nerve cells

Epithelium

- The covering tissue
- It lines all the exposed surfaces of the body, both exterior & interior
- It covers the skin, the blood vessels, the abdominal, chest cavities & GI tract

Connective & Supporting Tissue

- It binds tissue & organs together
- *Composition:*
    - High in protein
    - Fibers
- *Characteristic:* highly elastic
- *Examples:* bone ligaments & cartilage

Muscle Tissue

- A special type of tissue that can contract
- *Composition:* high in protein content

Nervous Tissue

- The avenue by which electrical impulses are transmitted throughout the body for control & response
- Composed of specialized cells *neurons*

Parenchymal

- Part of an organ that contains tissues representative of that particular organ

Stromal

- Part of an organ that is composed of connective tissue & vasculature

- *Function:* provides structure to the organ

Radiosensitivity of Tissues & Organs

- Determined by the function of the organ in the body
- The rate at which cells mature within the organ
- The inherent radiosensitivity of the cell type

RELATIVE RADIOSENSITIVITY OF TISSUES & ORGANS BASED ON CLINICAL RADIATION ONCOLOGISTS

LEVEL OF RADIOSENSITIVITY	TISSUE OR ORGAN	EFFECTS
High 200 to 1000 rad (2 to 10 Gy_t)	Lymphoid tissue	Atrophy
	Bone marrow	Hypoplasia
	Gonads	Atrophy
Intermediate 1000 to 5000 rad (10 to 5 Gy_t)	Skin	Erythema
	Gastrointestinal tract	Ulcer
	Cornea	Cataract
	Growing bone	Growth arrest
	Kidney	Nephrosclerosis
	Liver	Ascites
	Thyroid	Atrophy
Low > 5000 rad (> 5 Gy_t)	Muscle	Fibrosis
	Brain	Necrosis
	Spinal	Transaction